REMARKS

Reconsideration is requested.

Claims 42-70 have been canceled, without prejudice. Claims 71-96 have been added and will be pending upon entry of the above Amendment. Entry of the above amendments will place the application in condition for allowance. At a minimum, the amendments reduce the issues for appeal, such as the Section 112, second paragraph, rejections of various claims. Entry of the above amendment is requested.

The Examiner's helpful and extensive comments in the Office Action of February 22, 2002 (Paper No. 14) are acknowledged, with appreciation. The claims have been rewritten, as suggested by the Examiner on page 3 of Paper No. 14, to remove the objected-to language. Entry of the above amendments and withdrawal of the objection of claims 42-70 and Section 112, second paragraph, rejections of the claims indicated on pages 3-8 of Paper No. 14 are requested.

The Section 102 rejection of claims 42, 44-45, 49, 51-52, 54-56, 58, 60-61 and 65-69 over Barrett (Journal of General Virology, Vol. 71, 1990, pages 2301-2306) will be moot upon entry of the above amendments. The amended claims are submitted to be patentable over Barrett which fails, for example, to teach a cell substrate for the production of human vaccines. Specifically, the applicants believe that tumor derived HeLa cells of Barrett are not suitable in the presently claimed process. As Barrett fails to

teach each and every aspect of the presently claimed invention, the claims are submitted to be novel over Barrett.

The Section 103 rejection of claims 42-70 over Barrett will be moot upon entry of the above amendments. The applicants believe the above claims are patentable over Barrett as the claimed invention is submitted to be more than a mere obvious optimization of methods of Barrett. Specifically, the applicants note that Barrett was not concerned with production of a vaccine for human use such that the HeLa cells of Barrett would not have been acceptable in the presently claimed invention.

The applicants believe that the subconfluent monolayers of HeLa cells of Barrett were infected at a multiplicity (i.e., multiplicity of infection) of five, which represents the amount of virus in relation to the cells, which is considered very high for the production of human vaccines. To the contrary, the applicants claimed invention requires a concentration of infectious units per cell of 0.2-0.0001. This substantially lower multiplicity of infection advantageously and unexpectedly makes possible the utilization of the presently claimed process on a larger scale. This would not have been expected from the cited art.

The virus production process of Barrett was conducted in a manner wherein the interferon affect did not occur such that the problems faced by the applicants were not discussed or raised by Barrett and hence the solution was not obvious in view of Barrett. The applicants however discovered that the infectious virus yield per milliliter is inversely related to the cell seeding density. At high cell seeding densities, no cytopathology was observed while at low densities total cell death was observed. At

intermediate densities, partial cytopathology was observed. Thus, according to the present invention, the cell density range evades the interferon system and efficient production may be realized.

The applicants submit that one of ordinary skill in the art would have believed that an increase in cell density would produce an increase in virus yield whereas the applicants have discovered otherwise and the presently claimed invention is submitted to be patentable over the cited art.

In view of the above, the claims are submitted in condition for allowance and a Notice to that affect is requested.

Respectfully submitted,

NIXON & VANDERHYE P.C.

By: _____

B. J. Sadoff
Reg. No. 36,663

BJS:plb
1100 North Glebe Road, 8th Floor
Arlington, VA 22201-4714
Telephone: (703) 816-4000
Facsimile: (703) 816-4100